




Favourable course in a cohort of Parkinson's disease patients infected by SARS-CoV-2: a single-centre experience

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Received: 14 October 2020 / Accepted: 14 December 2020 / Published online: 13 January 2021
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Abstract

The COVID-19 outbreak has had a dramatic impact on the healthcare system due to the rapid, worldwide spread of the virus, highlighting several considerations on the best management of infected patients and also potential risks and prognostic factors in patients with pre-existing chronic diseases exposed to the virus. Neurodegenerative disorders are known to be chronic, disabling diseases that imply a higher vulnerability to infections, and for this reason, it has been suggested that SARS-CoV-2 infection may have a worse course in these patients. In the present study, we report our experience with 12 patients affected by Parkinson's disease (PD) who became infected with SARS-Cov-2 due to a COVID-19 outbreak in a care residency, and thus hospitalised in our COVID hospital. Most of the PD patients had a long disease duration and multiple comorbidities even though SARS-CoV-2 manifestations were mild, and none required intensive care. Despite lung conditions, most of our PD patients had mild symptoms: 7 patients were clinically asymptomatic (58.3%); 3 patients had fever, cough, and myalgia (25%) and 2 patients had dyspnoea (16%) that needed high-flow oxygen therapy. Few complications related to PD were seen. All patients were discharged after a mean hospitalisation period of 30 days. Mortality rate during hospitalisation was zero. Our findings suggest that SARS-CoV-2 infection does not have a poor prognosis in patients with PD. More extensive data and evaluations, however, are needed to confirm our data, and caution is warranted.

Keywords COVID-19 · SARS-CoV-2 · Parkinson's disease · Clinical outcome

Introduction

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan City, capital of Central China's Hubei Province, as the cause of a serious respiratory illness. The etiological agent of COVID-19 is designated as 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2). It belongs to the genus β -coronavirus together with SARS coronavirus (SARS-CoV)

and Middle East respiratory syndrome coronavirus (MERS-CoV) and is responsible for atypical pneumonia [1, 2]. A few months after the first report, the virus had spread worldwide, becoming a pandemic.

SARS-CoV-2 is a single-stranded positive-sense RNA virus and uses angiotensin-converting enzyme 2 (ACE2) receptors for entry into target cells that are expressed in the lungs, heart, intestinal tract, kidney, and in the brain.

The virus is transmitted via droplets and fomites during close unprotected contact, and transmission can occur during the pre-symptomatic phase.

COVID-19 may present similar to influenza, and the main clinical manifestations can include fever, non-productive cough, myalgia, loss of smell and taste, diarrhoea, headache and fatigue. Although most patients infected with SARS-CoV-2 are asymptomatic or develop mild to moderate symptoms, a subset of patients develops pneumonia and severe dyspnoea that can evolve to acute respiratory distress syndrome (ARDS) and require intensive care. COVID-19 severity increases with some risk factors such as age, hypertension,

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cardiovascular and cerebrovascular disease, diabetes and immunosuppression [3, 4].

Diverse reports have shown that COVID-19 patients may experience some neurological complications during the acute phase of the disease in association with the most common and life-threatening respiratory symptoms. Neurological manifestations include encephalopathy, agitation, confusion, seizure, acute cerebrovascular attacks and, more rarely, peripheral nervous system involvement with neuropathic pain, taste and smell impairment. It would appear that neurological symptoms are more pronounced in patients with severe infection [5].

Furthermore, the impact of COVID-19 on patients with a pre-existing neurological disorder, whether acquired or inherited, is another important issue that neurologists have had to face in recent months, but real data are poor. For instance, it has been suggested that patients with chronic diseases may have a worse outcome due to their fragility, and this is the case for the majority of neurodegenerative diseases, implying that patients suffering from a disabling neurological disorder manifest a higher risk to developing a severe course of COVID-19.

Parkinson's disease (PD) is a neurodegenerative disease characterised by early death of dopaminergic neurons in the substantia nigra pars compacta (SNpc). Dopamine deficiency leads to common parkinsonian motor symptoms (bradykinesia, rigidity, rest tremor, postural instability) and non-motor symptoms (olfactory dysfunction, cognitive impairment, dementia and depression, sleep disorders, autonomic dysfunction) [6].

PD patients, especially in the advanced phase, are quite disabled and receive polytherapy, and their clinical condition is often aggravated by multiple comorbidities with implications in daily life management.

There are a number of papers that speculate on possible links between COVID-19 and PD in terms of aetiologies, risk and consequences [7]. So far, not enough data support more susceptibility to COVID-19 in PD or the likelihood of developing PD because of SARS-CoV-2 infection. There are few neuropathological studies, and these do not demonstrate if the virus is able to directly infect the brain. In addition, the expression of ACE2 receptors, the major point of entry for the virus, in neurons is not well elucidated, but some evidence shows that ACE2 receptors are expressed in dopamine neurons and are significantly reduced in PD due to the degenerative process [8].

Not clear evidence is reported on a greater risk of SARS-CoV-2 in patients with PD although some reports have suggested that patients affected by PD and COVID-19 may have a worse outcome. Two different movement disorder groups reported on 10 PD patients with COVID-19 from the Padua Parkinson's Disease Movement Disorders Centre and London King's College Hospital. According to clinical data and their

outcomes, they suggest there is a major susceptibility to COVID-19 in PD patients of older age and with longer disease duration and show a high mortality rate especially in patients who have undergone advanced therapies [9].

The aim of this study is to describe our observations on a population of patients with PD and COVID-19 admitted to the COVID Hospital at AOU Policlinico G. Martino of Messina.

Materials and methods

We collected, retrospectively, clinical data on patients hospitalised for SARS-CoV-2 pneumonia between 08 March 2020 and 30 May 2020 at the COVID Hospital at AOU Policlinico G. Martino of Messina.

The study was approved by the Ethic Committee of AOU Policlinico Universitario di Messina.

COVID-19 infection was defined as a rhinopharyngeal swab revealing a positive result in reverse transcription quantitative PCR assay. It was diagnosed on the basis of WHO guidelines [2]. Data from 140 COVID-19 inpatients were collected in an extensive database that included patient demographics (age, sex, ethnicity) comorbidities at admission, such as history of smoking, hypertension, cardiovascular disease (arrhythmia, congestive heart failure, coronary artery disease), diabetes, hyperlipaemia, chronic obstructive pulmonary disease (COPD), kidney failure, neurological degenerative or cerebrovascular disease, cancer, pre-existing dysimmune disorders and use of immunomodulant drugs or other previous medications. We also collected clinical data related to COVID-19 infection such as clinical manifestations, laboratory investigation, chest X-Ray, type of treatment used, need of oxygen therapy and data on clinical course such as length of stay, outcome and discharge status.

Clinical data on patients with known diagnosis of PD at admission were analysed focusing on outcome in terms of clinical status at admission and during hospitalisation, duration and severity of PD and clinical manifestations related to SARS-CoV-2 infection (symptoms and severity). Additional parameters were considered including therapeutic implementation of PD drugs, disease complications, type of discharge and mortality. Clinical status for PD patients was assessed according to the modified Hoehn and Yahr (H&Y) Scale and Unified PD Rating Scale (UPDRS). Both scales were administered at admission and during observation.

Results

Out of 140 patients admitted to the COVID Hospital at AOU Policlinico "G. Martino" of Messina, between 8 March 2020 and 30 May 2020 because of SARS-CoV-2 pneumonia, 12 patients (11.2%) had a previous diagnosis of PD.

All PD patients at the time of infection were either hospitalised in a Rehabilitation Centre (9/12 pts) or in a Nursing Home (3/12). Six patients (50%) were female; age ranged from 58 to 87 years (mean age 73 years).

On admission at our hospital, a nasopharyngeal swab detected with real-time (RT)-PCR revealed the presence of coronavirus RNA compatible with SARS-CoV-2 infection. Chest X-ray was performed on all patients, showing interstitial pneumonia. Despite lung conditions, most of our PD patients had mild symptoms; in particular, 7 patients were clinically asymptomatic (58.3%), 3 patients had fever, cough and myalgia (25%); among them, one patient also had headache. Two patients had dyspnoea (16%) that needed high-flow oxygen therapy. Most of the patients had insomnia and suffered from mild anxiety.

PD duration was between 4 and 22 years (median 22 years); all patients, except one, were treated with levodopa in monotherapy or in variable association with ropinirole and/or rasagiline, safinamide, tolcapone and opicapone. Two patients had undergone advanced therapies; one had deep brain stimulation (from 2018) and one with levodopa in continuous infusion therapy. Only one patient was without specific treatment (see Table 2).

Neurological examination showed relevant motor dysfunctions and resting and postural tremor, and some had postural and balance impairment with falling and cognitive impairment. None of the patients had dystonic symptoms. Mean H&Y scale was 3.8 (range 2.5–5); mean UPDRS scale was 57 (range 27–105).

In terms of comorbidity, 5 patients (41.6%) had hypertension, 8 (66.6%) cardiovascular disease, 2 (16.6%), 1 (8.33%) COPD, 1 (8.33%) hyperlipaemia and 3 (25%) chronic kidney failure (Table 1).

Considering the course of PD, a worsening or appearance of new symptoms, the patients were quite stable. No patient needed drug implementation except in one case during hospitalisation, one (8.33%) patient presented hallucinatory phenomena treated with quetiapine therapy. UPDRS score increased from 54 to 58.

Regarding the treatment against SARS-CoV-2 infection, all patients were given anticoagulant therapy with enoxaparin subcutaneous at a dosage of deep vein thrombosis prophylaxis; 4 out of 12 subjects (33.3%) were given combination therapy with hydroxychloroquine (200 mg TID for the first day and 2000 mg die for 9 days) and azithromycin (25 mg TID for a day and 25 mg die for the following 4 days).

The mean length of hospitalisation was 30.6 days. Mortality rate was zero.

Discussion

The COVID-19 pandemic has had a dramatic impact on healthcare systems and has prompted a reconsideration worldwide of some priorities in medical care. Although many issues

Table 1 Demographic and clinical characteristics of PD patients

Demographic data	
Sex - <i>n.</i> (%)	
Female	6 (50)
Male	6 (50)
Age - <i>n.</i> (%)	
< 55	0
55 - 65	3 (25)
66 - 75	2 (16.6)
76 - 85	4 (33.3)
> 85	2 (16.6)
Other Comorbidities - <i>n.</i> (%)	
Hypertension	5 (41.6)
Cardiovascular disease	8 (66.6)
Diabetes	2 (16.6)
COPD	1 (8.33)
IRC	3 (25)
Symptoms of COVID-19 - <i>n.</i> (%)	
Fever	4 (33.3)
Cough	2 (16.6)
Dyspnoea	1 (8.33)
Diarrhoea	0
Hypogeusia	0
Hyposmia	0
Headache	4 (33.3)
Treatment - <i>n.</i> (%)	
Antiviral treatment	4 (33.3)
Oxygen therapy	2 (16.6)
Days of hospitalization - average	30.7
Death in hospital - <i>n.</i> (%)	0

have yet to be clarified on the infection, it is evident that most patients are asymptomatic or develop only mild upper respiratory symptoms whereas elderly patients with chronic comorbidities are more vulnerable to developing severe manifestations including acute respiratory distress and the risk of poor outcome [3].

In the present study, we report our experience on a group of patients with PD who were infected with SARS-CoV-2 due to a COVID-19 outbreak in a care residency and thus hospitalised in our COVID hospital.

From 8 March 2020 to 30 May 2020, we collected data on 140 patients admitted to the COVID hospital of the AOU Policlinico G Martino of Messina. Among them, 12 had a previous diagnosis of PD. The majority were first hospitalised at a rehabilitation centre where a COVID-19 infection outbreak had developed. PD patients were hospitalised for SARS-CoV-2 pneumonia. Clinical symptoms of COVID-19 were not critical; they had a mild to moderate clinical course

Table 2 Clinical features and outcome of PD Patients with COVID-19

Patient	Age	Sex	Year of PD diagnosis	PD therapy	UPDRS	HY	Comorbidities	Symptoms of COVID-19	Treatment for COVID-19	Length of stay (days)	Discharge status
1	76	M	2016	Levodopa Carbidopa- Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	44	4	Benign prostatic hyperplasia	None	Enoxaparin	27	Discharged home
2	60	M	2000	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	105	5	none	Fever Fatigue Myalgia	Enoxaparin	30	Discharged home
3	67	F	2013	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	54	3	Atherosclerosis Osteoporosis Multinodular goitre	None	Enoxaparin	17	Discharged home
4	58	M	2005	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	57	4	None	Fever Fatigue Headache Myalgia	Azithromycin HCQ Enoxaparin	17	Discharged to rehabilitation facility
5	58	M	2014	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	50	4	Hypertension	None	Enoxaparin	46	Discharged home
6	76	M	2005	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	54	4	Hypertension Diabetes, Benign prostatic hyperplasia	None	Enoxaparin	50	Discharged to rehabilitation facility
7	70	F	2004	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	27	2.5	Hypertension	None	Enoxaparin	23	Discharged home
8	81	M	2003	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	57	3	HCV	Dyspnoea fever Myalgia Fatigue Fever	High-flow oxygen therapy Enoxaparin Enoxaparin		
9	76	F	2015	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	59	3	Glaucoma Hypertension Diabetes	Dyspnoea Fever	High-flow oxygen therapy Enoxaparin Enoxaparin	23	Discharged home
10	87	F	2000	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	100	5	Chronic kidney disease	Dyspnoea Fever	High-flow oxygen therapy Enoxaparin Azithromycin HCQ	36	Discharged to home nursing care
11	84	F	1998	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	59	4	Ischemic cardiopathy	None	Enoxaparin	38	Discharged to home nursing care
12	87	F	2005	Levodopa Carbidopa Benserazide Rasagiline Opicapone STN DBS since 2008 Rasagiline Levodopa + benserazide Clonazepam Tolcapone	41	4	Hypertension Previous stroke	None	Enoxaparin Azithromycin HCQ		Discharged to home nursing care

STN subthalamic nucleus, DBS deep brain stimulation, UPDRS Unified Parkinson's Disease Rating Scale, HY Hoehn and Yahr, HCQ hydroxychloroquine

of COVID-19 infection, with no respiratory distress. Only two patients needed high flow of oxygen therapy, but no one needed hospitalisation in the intensive care unit. PD disease duration was variable, ranging from 4 to 22 years but 8/12 had a clinical history > 10 years. All patients were taking complex therapies with high dosage of L-dopa, MAO inhibitors, and dopamine agonists; one had deep brain stimulation, and another was on L-dopa in continuous infusion. Neurological impairment was mild to severe according to scores on the rating scales (Table 2). Some patients had pre-existing multiple comorbidities at admission. However, PD patients did not show any deterioration of pre-existing neurological conditions or evidence of new symptoms (except in one patient who experienced episodes of hallucinations). No implementation or modification of PD-related drug therapy was carried out.

Despite the presence of one or more comorbidities (diabetes, hypertension, heart disease, hyperlipidaemia, COPD, previous cancer), all the patients were discharged, after a mean hospitalisation period of 30 days, home (if possible) or to a rehabilitation centre. Mortality rate during hospitalisation was zero.

Over the past 11 months, physicians and scientists with expertise in PD have gathered their preliminary data on the experience of people with PD affected by COVID-19. Literature focused on two aspects: data regarding the experience of people with PD during the early era of the COVID-19 pandemic as it impacted on their daily lives, not directly related to the virus infection, and reports regarding people with PD who have contracted COVID-19 [10–12].

Diverse studies report on the impact of COVID-19 on the disease course of PD, and taken together, it can be concluded that mortality due to COVID-19 among people with PD correlates with the more advanced stage of the disease. Motor and non-motor symptoms increased during the COVID-19 lockdown in people with PD who did not contract COVID-19, whilst people with PD who contracted COVID-19 often reported new or worsening motor and/or non-motor symptoms in the setting of their illness [9, 13, 14].

Considering the small number of patients, we cannot perform statistical analyses but based on real data, our patients appear to have had a benign course of the infection that apparently did not impact negatively on the pre-existing clinical condition.

Similar results were reported in a community-based control study, comparing PD patients, with and without COVID-19, who showed significantly worsened motor and non-motor symptoms in the COVID-19 group, requiring therapy adjustment in one third of cases, with urinary issues and fatigue as the most prominent non-motor issues. However, comparing our cohort with PD patients reported in the community-based study, COVID-19 was moderate in 66% of patients and mainly managed at home by the general practitioner; only 1 patient

was hospitalised (8.3%) as a result of pneumonia. Also, in this context, the mortality rate was zero [14].

With regard to the mortality risk, a very recent study, from the TriNetX-COVID-19 database, found that COVID-19-related fatality rates (CFR) increased in PD patients, independent of age, sex and race. Despite the high number of patients recruited, some relevant limitations, such as numerosity of Healthcare Provider Centres, no information in the database regarding comorbidities and recovery, may impact the research findings [15].

In our report, the observational study design and the heterogeneity of population cannot exclude confounding factors. Probably, the high percentage of people with PD affected by COVID-19 is related to the previous hospitalisation in a rehabilitation centre (where an infectious outbreak occurred and caused the infection); if PD patients stay in their home, taking common precautionary measures, adopting hygienic and spacing measures and social isolation, they may avoid COVID-19 infection. However, we observed that despite the radiological findings of interstitial pneumonia, PD patients had a favourable clinical course. Only in two cases did we detect a mild to moderate respiratory syndrome with the need for oxygen therapy. No one required emergency treatment in an intensive care unit.

Despite the limitations of our study, in our experience, patients with PD and COVID-19 infection had a favourable course and did not show a higher severity of SARS-CoV-2 disease or worsening of known neurological disease compared with the general population as was previously suggested. Further research and larger studies are necessary to confirm our observations. According to the data already reported, including ours, it is recommended that the management of PD patients who contract COVID-19 during infection be personalised, and also after recovery to better elucidate the real consequences on the clinical course of PD.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval None.

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